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Oral D-Methionine Provides Cisplatin Otoprotection as Effectively as Intraperitoneal D-Methionine in Rats

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Cisplatin is an anti-cancer drug that can cause permanent hearing loss. The sulfur-based amino acid D-methionine (D-met) is an antioxidant that can protect against cisplatin-induced ototoxicity. Multiple animal studies have shown that systemic D-met protects the organ of Corti, and stria vascularis from cisplatin without significant interference with cisplatin's anti-tumor action or apparent side effects when administered appropriately. The goal of this study was to determine whether oral D-met is as effective as injected D-met in providing cisplatin otoprotection. Male Wistar rats were divided into 6 groups of 5 animals each. Group 1 comprised a normal control group receiving saline injection only. Group 2 comprised a treated control group given a 30-minute i.p. infusion of 16 mg/kg cisplatin. Group 3 received 1000 mg/kg (200mg/ml concentration) oral D-met delivered by gavage 2 hours before infusion of 16 mg/kg cisplatin. Group 4 received 300 mg/kg D-met delivered i.p. 30 minutes before cisplatin infusion. This i.p. D-met dose is known to fully protect against cisplatin-induced ABR threshold elevations. Group 5 received 300 mg/kg D-met delivered i.p. only. Group 6 received 1000 mg/kg (200 mg/ml concentration) D-met delivered orally by gavage. Auditory brainstem response (ABR) data collection was obtained at baseline just prior to drug delivery and again 3 days after drug administration centered at frequencies of 4, 8, 14, 20, and 30 kHz. An intensity series was obtained for each animal from 100 to 0 dB sound pressure levels (SPL) for tone bursts in 10 dB decrements. Post-treatment ABR thresholds were significantly higher for the cisplatin alone group than for any other group, and none of the D-met groups yielded findings significantly different from those of the saline alone controls. Histology is in progress. We conclude that D-met taken orally is as effective as injected D-met at preventing cisplatin-induced ABR threshold elevation in rats.